



Complete Summary

GUIDELINE TITLE

American Gastroenterological Association medical position statement: parenteral nutrition.

BIBLIOGRAPHIC SOURCE(S)

American Gastroenterological Association medical position statement: parenteral nutrition. Gastroenterology 2001 Oct;121(4):966-9. [1 reference]

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SCOPE

DISEASE/CONDITION(S)

Protein energy malnutrition

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness

CLINICAL SPECIALTY

Critical Care
Family Practice
Gastroenterology
Internal Medicine
Oncology
Pediatrics
Surgery

INTENDED USERS

Dietitians
Physicians

GUIDELINE OBJECTIVE(S)

To assess the clinical efficacy of parenteral nutrition

TARGET POPULATION

Patients who are unable to obtain adequate nutrients by oral or enteral routes and who may be at risk for malnutrition

INTERVENTIONS AND PRACTICES CONSIDERED

1. Parenteral nutrition
2. Protein-sparing therapy

MAJOR OUTCOMES CONSIDERED

- Mortality
- Total complication rate
- Infectious complication rate
- Duration of hospitalization
- Cost

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Since 1974, one of the authors of the technical report has been collecting randomized controlled trials in the field of nutritional support. To date, over 1000 references have been identified. This collection was created by using the following strategies:

- Manual search of Index Medicus
- Manual search of individual journals (including abstracts from various society meetings)
- References of identified papers
- Personal contacts with other investigators
- A computer search of the Cochrane Library (1999, issue 3)
- A computer search of Embase

NUMBER OF SOURCE DOCUMENTS

82 trials meeting inclusion criteria for parenteral nutrition

27 trials evaluating protein-sparing therapy

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Subjective Review

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis of Randomized Controlled Trials
Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Inclusion criteria: Any randomized controlled trial (RCT) (including one only reported as an abstract) that met the following criteria was used in the meta-analysis:

1. The report explicitly stated that the patient groups were randomized. Quasi-randomized trials (allocation based on day of week, record number, or some other system whereby the group assignment was known by the investigator and/or subject before accession into the trial) were excluded.
2. The study compared treated patients (those receiving intravenous fluids containing a source of nitrogen (as amino acids or protein hydrolysate) and at least $10 \text{ kcal} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$ of nonprotein calories) to control patients, who received no nutrient intake beyond that contained in ad libitum feedings and/or 5% (or in the case of neonatal trials, 10%) dextrose intravenously as maintenance fluid.
3. The study reported one or more outcomes of mortality, morbidity, duration of hospitalization and/or cost.

A separate meta-analysis of protein-sparing therapy, a form of intravenous nutrition in which nitrogen was infused along with an amount of calories that was inadequate to meet the daily requirement ($<10 \text{ kcal} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$), is included.

For a variety of reasons, other RCTs were not included in these meta-analyses. These studies, as well as the reasons for exclusion, are listed in the Appendix of the Technical Review.

Outcome assessment: Each identified RCT was categorized by clinical condition and reviewed for outcomes of mortality, total complications, infectious complications, duration of hospitalization, and cost. For each clinical condition itemized in Table 1 of the technical report, data regarding disease-specific

outcomes were also identified when available. Data from each RCT were abstracted twice, and differences were resolved by consensus.

When a report included more than one eligible treatment arm, each treatment group was compared with the common control group and considered to be a separate trial. When data were presented as the total number of events, rather than the number of patients who had that event, it was assumed that there was one event per patient. (If the number of events was greater than the number of patients, it was assumed that each patient had at least 1 such event.) When data were presented in graphic, rather than tabular, form, numerical data were estimated from the graph.

Some endpoints (e.g., mortality) have low occurrence rates; differences can only be detected if large numbers of patients are available. Other outcomes (e.g., duration of hospitalization) have low rates of reporting. To detect such effects of parenteral nutrition or protein sparing therapy, global meta-analyses of all the eligible trials were performed. Meta-analysis was performed only when data were available from at least 3 trials. Thus, the calculations were performed only in the following sets of RCTs:

1. A global meta-analysis of all eligible trials (both parenteral nutrition and protein sparing)
2. Perioperative trials (both parenteral nutrition and protein-sparing therapy meta-analyses)
3. Oncologic therapy trials (cancer chemotherapy, radiation therapy, and bone marrow transplantation; only parenteral nutrition meta-analysis)
4. Alcoholic hepatitis trials (only protein-sparing therapy meta-analysis)
5. Low-birth-weight infants trials (only parenteral nutrition meta-analysis)

For dichotomous variables (mortality and morbidity events), each estimated effect is presented as the absolute risk difference (the difference between the incidence in the treated group and the incidence in the control group) and 95% confidence interval. A negative risk difference indicates that there is a decreased risk, and a positive one indicates that there is an increased risk associated with the treatment. A significant effect is present whenever a 95% confidence interval does not overlap 0. The number needed to treat to prevent (or cause) one outcome event is calculated by dividing 100 by the absolute risk difference. For example, if the risk difference for a particular complication were -5%, it would be necessary to treat 20 patients to prevent one such event. Similarly, if the risk difference were +5%, treating 20 patients would result in one additional complication.

Because heterogeneity was anticipated, all of the meta-analyses were performed using a random effects model. The computer programs used were Revman 4.0.4 and Metaview 3.1 (Cochrane Collaboration, Oxford, England).

Subgroup analyses: For each of the outcomes in the parenteral nutrition meta-analysis, separate calculations were undertaken to assess the following factors:

1. Use or non-use of lipid in the parenteral nutrition formulation. Nutritional support was considered to include lipid if at least 15% of total nonprotein calories in the nutritional formulation were derived from lipid. Non-use of lipid meant either that no lipid was provided or that only small amounts of lipid

- (<15% of the total nonprotein calories) were used periodically, usually to prevent essential fatty acid deficiency.
2. Presence or absence of malnutrition in the study population. A trial was considered to contain malnourished patients if at least 50% of the patients satisfied the investigators' definition of malnutrition at entry. A trial was considered not to contain malnourished patients if <50% of the patients satisfied this criterion. Malnutrition was variably defined in these trials, and those definitions ranged from modest weight loss alone to more profound weight loss, and/or hypoalbuminemia, and/or abnormalities in anthropometric measurements, or skin test reactivity.
 3. Inclusion of only those trials that were reported in full paper form (i.e., not just as an abstract).
 4. Inclusion of only those trials in which the nutritional therapy was provided for at least 7 days.
 5. Inclusion of only those trials that reported outcome events as the number of affected patients (i.e., not just as total number of events).
 6. Provision of parenteral nutrition only in the preoperative period, only in the postoperative period, or in both.
 7. Provision of parenteral nutrition only for patients undergoing surgery for upper gastrointestinal cancer. (This subgroup analysis was the only one not determined a priori.)
 8. Provision of parenteral nutrition for patients treated with chemotherapy, radiation therapy, or bone marrow transplantation.

The authors were unable to perform such subgroup analyses in the meta-analysis of protein-sparing therapy for the following reasons:

1. The caloric content was not an issue.
2. Preoperative or pretreatment nutritional status was not usually reported or was normal.
3. All but 1 RCT was published as a full paper.
4. Almost all of the surgical trials provided postoperative protein-sparing therapy for <7 days, and all of the trials in alcoholic hepatitis used it for more than 1 week.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The recommendations range from A-E:

- A: Therapy should be used routinely
- B: Therapy probably should be used routinely
- C: No randomized controlled trial evidence to assess whether or not therapy should be used
- D: Therapy probably should not be used
- E: Therapy should not be used routinely

COST ANALYSIS

All of the randomized controlled trials used in the meta-analysis were reviewed for a number of outcomes, including cost. When adequate cost data were available, a meta-analysis regarding cost was performed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This document was approved by the Clinical Practice and Practice Economics Committee on April 13, 2001, and by the American Gastroenterological Association Governing Board on May 18, 2001.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the range of recommendations (A-E) are repeated at the end of the Major Recommendations.

Overview

In general, parenteral nutrition is indicated to prevent the adverse effects of malnutrition in patients who are unable to obtain adequate nutrients by oral or enteral routes. However, the duration of starvation or semistarvation that can be tolerated by each patient before adverse effects occur is not clear, and probably depends on the amount and type of inadequate nutrient intake, the amount of available endogenous fuel stores (adipose tissue triglycerides), muscle mass, and the rate of endogenous fat and muscle protein catabolism. Therefore, the decision to use parenteral nutrition requires an understanding of the patient's clinical condition and anticipated outcome, judgment as to the patient's ability to tolerate undernutrition, knowledge of the data evaluating the clinical efficacy of parenteral nutritional support from pertinent clinical trials, and an appreciation of the desires and needs of the patient and his or her family.

Specific Clinical Conditions

Perioperative period

1. Parenteral nutrition given before or after surgery may slightly reduce the number of postoperative complications, but the benefit of this therapeutic approach is unlikely to justify the costs. Therefore, parenteral nutrition should not be routinely administered to most surgical patients. (D)
2. Preoperative parenteral nutrition has a more profound effect in reducing the rate of major postoperative complications in patients undergoing major surgery for cancer of the esophagus or stomach. As such, it should be used in such individuals if its costs are largely compensated by the reduced suffering and by the lessened resource utilization gained by avoiding the anticipated complications. (B)

3. Preoperative parenteral nutrition should also be considered in those patients who are severely malnourished (as defined in the technical review document). A retrospective subgroup analysis of one large randomized controlled trial (RCT) suggests that it does have a greater therapeutic effect in decreasing postoperative complications in this group.

Oncologic conditions

1. Parenteral nutrition should not routinely be given to patients undergoing cancer chemotherapy or radiation therapy because it increases the risk of complications and impairs the response to treatment. (E)
2. The indications for parenteral nutrition in patients undergoing bone marrow transplantation are unclear because of conflicting data regarding mortality. The decision to use it or not during the time of transplantation will have to be made by the responsible physician in the absence of any clear direction from RCTs. (C)

Liver disease

1. Although parenteral nutrition may improve liver function tests, it does not alter morbidity or mortality rates in patients with alcoholic hepatitis. It should not be used routinely in such patients. (D)
2. Branched-chain amino acid-enriched solutions are beneficial in improving hepatic encephalopathy in patients with cirrhosis. However, their expense (compared with alternative therapies) will limit their utility. (B)
3. There are no data available from RCTs in other liver diseases. The decision regarding using or not using parenteral nutrition in those conditions will be left to the judgment of the physician. (C)

Acute pancreatitis

1. Parenteral nutrition should not be given routinely to patients with mild acute pancreatitis, because it increases the cost and duration of hospitalization and may increase the risk of infectious complications. (E)
2. There are no data from RCTs to provide direction regarding if and when to use parenteral nutrition for patients with more severe pancreatitis. Decisions about its utilization or nonutilization in such patients must be left to the discretion of the responsible physician. (C)

Inflammatory bowel disease

1. Parenteral nutrition does not increase the rate of remission or decrease the need for surgery in patients with acute colitis. It should not be used routinely. (D)
2. Indirect evidence suggests that parenteral nutrition is less effective than steroid therapy in treating active Crohn's disease. As such, it should not be used routinely. (D)
3. Bowel rest is not necessary to achieve clinical remission in patients with exacerbations of inflammatory bowel disease.

Low-birth-weight infants

1. Parenteral nutrition should not be used if oral or enteral nutrient delivery is possible. (D)
2. If oral or enteral nutrient delivery is not feasible, parenteral nutrition will be necessary because of the limited nutritional reserves in these infants. (A)

Acquired immunodeficiency syndrome

Data from one long-term study and the expense and potential for infection indicate that routine long-term parenteral nutrition should not be used. (D)

Pulmonary disease

Data from two RCTs and the inferential evidence from other disease states (including data from critically ill patients on mechanical ventilation) indicate that parenteral nutrition is not effective. It should not routinely be administered during acute exacerbations or for long-term outpatient care. (D)

Renal disease

There are no RCTs comparing parenteral nutrition to standard therapy. The decision to use it or not must be made by the responsible physician without the benefit of such data. (C)

Burn injury

1. Parenteral nutrition is associated with higher mortality than enteral nutrition. Therefore, the routine use of parenteral nutrition is contraindicated if enteral routes of feeding are available. (E)
2. In the absence of available enteral routes, the decisions of whether and when to use, or not to use, parenteral nutrition must be made without the benefit of data from RCTs. (C)

Other critical illnesses

1. The data from one small trial and the experiences in other disease states indicate that parenteral nutrition is not beneficial in patients with trauma. As such, it should not be used routinely. (D)
2. The duration of mechanical ventilation is not shortened by parenteral nutrition. Parenteral nutrition should not be used for this reason. (D)

Protein-sparing therapy

Hypocaloric nitrogen-containing intravenous infusions do not provide clinical benefits. Protein-sparing therapy should not be used routinely. (E)

Home parenteral nutrition

1. Long-term parenteral nutrition is indicated for patients with prolonged gastrointestinal tract failure that prevents the absorption of adequate nutrients to sustain life. (A)

2. Home parenteral nutrition should not be provided to patients with limited life expectancies (less than 3 months). (E)

Protracted periods of inadequate nutrient intake

1. Patients who are not severely malnourished can likely tolerate at least 1 week of starvation without adverse effects. Parenteral nutrition should not, therefore, be provided to patients who are expected to receive adequate oral or enteral feeding within 1 week. (E)
2. The duration of time that a patient who is not severely malnourished can tolerate inadequate nutrient intake beyond a week is unknown and may depend on the current nutritional status, the nature of the nutrient inadequacy, and the catabolic rate of the underlying disease. It is unknown at what time beyond 7 days such patients should begin parenteral nutrition if they cannot be fed enterally. As such, the decision to use it must be made by the responsible physician in the absence of direction from RCTs. (C)
3. It is unknown how long severely malnourished patients can tolerate inadequate nutrient intake. As such, the decision of whether and when to use parenteral nutrition must be made by the responsible physician in the absence of data from RCTs. (C)

Definitions:

The recommendations range from A-E:

A: Therapy should be used routinely

B: Therapy probably should be used routinely

C: No randomized controlled trial evidence to assess whether or not therapy should be used

D: Therapy probably should not be used

E: Therapy should not be used routinely

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations for parenteral nutrition are based on analysis of data from 82 randomized controlled trials that evaluated the efficacy of parenteral nutrition on one or more clinically important parameters of mortality, morbidity, duration of hospitalization, and/or cost. The recommendations for protein-sparing therapy are based on analysis of 27 other randomized controlled trials.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of parenteral nutrition

POTENTIAL HARMS

Complications of parenteral nutrition

Parenteral nutrition can cause serious complications related to mechanical aspects of line insertion, infections from contaminated solutions or inadequate catheter care, and metabolic abnormalities from inappropriate nutrient formulations. In addition, serious hepatobiliary and bone complications are associated with long-term parenteral nutrition. The risk of most complications that occur in the hospital is decreased when the administration of parenteral nutrition is supervised by an experienced nutrition support team.

Refeeding the severely malnourished

Aggressively refeeding patients who are severely malnourished can have adverse clinical consequences ("refeeding syndrome"), especially in the first few days. These potentially life-threatening complications include: (1) fluid overload and congestive heart failure (due to excessive fluid and sodium administration in conjunction with decreased cardiac mass and contractility); (2) serum electrolyte abnormalities (particularly hypophosphatemia and hypokalemia caused by insulin-stimulated tissue uptake from plasma); (3) cardiac arrhythmias (including ventricular tachyarrhythmias); and (4) glucose intolerance with hyperglycemia.

Global meta-analysis of parenteral nutrition

Parenteral nutrition was associated with a significant increase in the infectious complication rate; the absolute risk difference was +5%. Parenteral nutrition resulted in 1 additional infection for every 20 patients who were treated. In almost every subgroup analysis, the estimates were positive (treatment associated with more infections), although the confidence intervals sometimes overlapped 0. Significant differences were observed in the trials in which lipid was not used, in which only nourished patients were included, in which parenteral nutrition was provided for at least 7 days, and in the trials reported as full papers. This harmful effect was caused largely by the effect parenteral nutrition had in cancer patients receiving oncologic therapy. It was not observed when the perioperative or low-birth weight clinical conditions were separately analyzed.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Most of the randomized trials that were included in the analysis were not of high quality. However, low-quality studies tend to show more profound treatment effects. Thus, it is unlikely that the calculated effects of parenteral

- nutrition in the accompanying technical review represent major underestimations of its benefit.
- Virtually all of the trials included in the analysis excluded patients who were severely malnourished (defined by a large-percentage weight loss of a very low body index). The authors do not know if the results of these randomized controlled trials can be applied to severely malnourished patients.
 - Although a large number of randomized trials were available for the surgical and oncologic states, as well as for the trials of protein-sparing therapy, the recommendations for the other states were based on fewer studies. Future large trials could demonstrate beneficial effects that would change one or more of these recommendations. Nevertheless, any claims that certain subgroups of patients should be treated must be accompanied by proof of efficacy.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

End of Life Care
Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

American Gastroenterological Association medical position statement: parenteral nutrition. *Gastroenterology* 2001 Oct;121(4):966-9. [1 reference]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 May 18

GUIDELINE DEVELOPER(S)

American Gastroenterological Association - Medical Specialty Society

SOURCE(S) OF FUNDING

American Gastroenterological Association

GUIDELINE COMMITTEE

American Gastroenterological Association Clinical Practice and Practice Economics Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Not stated

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

An update is not in progress at this time.

According to the guideline developer, the Clinical Practice Committee meets 3 times a year to review all American Gastroenterological Association guidelines. This review includes new literature searches of electronic databases followed by expert committee review of new evidence that has emerged since the original publication date.

This guideline has been reviewed by the developer and is still considered to be current as of Dec 2001.

GUIDELINE AVAILABILITY

Electronic copies: Available from the [American Gastroenterological Association \(AGA\) Gastroenterology journal Web site](#).

Print copies: Available from American Gastroenterological Association, 4930 Del Ray Avenue, Bethesda, MD 20814.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Ronald L. Koretz; Timothy O. Lipman; and Samuel Klein. AGA technical review on parenteral nutrition. Gastroenterology 2001 Oct; 121(4):970-1001 [220 references].

Electronic copies: Available from the [American Gastroenterological Association \(AGA\) Gastroenterology journal Web site](#).

Print copies: Available from American Gastroenterological Association, 4930 Del Ray Avenue, Bethesda, MD 20814.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on June 5, 2002. The information was verified by the guideline developer on July 12, 2002.

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